UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/977,059	10/11/2001	Prasad V.V.S.V. Manchem	25352-0029	1824

25213 7590 03/23/2004

HELLER EHRMAN WHITE & MCAULIFFE LLP
275 MIDDLEFIELD ROAD
MENLO PARK, CA 94025-3506

EXAMINER	
JIANG, SHAOJIA A	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 03/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/977,059	MANCHEM ET AL.	
	Examiner	Art Unit	
	Shaojia A Jiang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/30/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 17, 2003 has been entered.

This Office Action is a response to Applicant's request for continued examination (RCE) filed December 17, 2003, and amendment and response to the Final Office Action (mailed June 18, 2003), filed December 17, 2003 wherein the instant specification has been amended as to page 3 regarding to the incorporation of US patents; claims 1-20 are cancelled; claims 21-36 are newly added.

Currently, claims 21-36 are pending in this application.

Claims 21-36 are examined on the merits herein.

Objection to the Specification

The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper, i.e., page 16 lines 10-14. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing

the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

The attempt to incorporate subject matter into the instant application by reference to other than US Patents is improper. Currently, the specification is objected to because the essential subject matters are incorporated herein by reference to other than US patents.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21-22 and 30-36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant's amendment with respect to newly added claims 21-36 has been fully considered but is deemed to insert **new matter** into the claims since the specification as originally filed does not provide support for those compounds

having Formula I in particular when Y is now newly defined in claim 21 and those particular compounds (subgenus and species) in claims 22 being useful in the instant method of treating a metabolic disorder in a person induced by treatment of the person with a HIV protease inhibitor, even though the compounds themselves when Y is now newly defined in claim 21 (subgenus) and those particular compounds (subgenus) in claims 22 taught in the US patent 6,458,998 incorporated herein by reference in the specification. However, the 6,458,998 merely discloses these compounds including subgenus and species themselves in claims 21-22 and their use in the methods of stimulating the kinase activity of the insulin receptor, activating the insulin receptor, or stimulating the uptake of glucose, but the patent within the four corners does not fairly provide the support for these particular subgenus and species being useful in the instant method of treating a metabolic disorder in a person induced by treatment of the person with a HIV protease inhibitor. It is noted that treating a metabolic disorder is much broader that treating diabetes in a person. The specification as originally filed merely discloses that the broad genus compounds of formula I when each Y is a non-interfering substituent are useful in the instant method (see page 4 of the specification). Thus, the specification as originally filed does not provide support the method of treating a metabolic disorder in a person induced by treatment of the person with a HIV protease inhibitor by administering these particular subgenus and species in 21-22, as noted in MPEP 2163, "a subgenus is not necessarily described by a genus encompassing it and a species upon which it reads", see *In re Smith*, 458 F.2d 1389, 1395, 173 USPQ 679, 683 (CCPA 1972).

Consequently, there is nothing within the instant specification which would lead the artisan in the field to believe that Applicant was in possession of the invention as it is now claimed. See *Vas-Cath Inc. v. Mahurkar*, 19 USPQ 2d 1111, CAFC 1991, see also *In re Winkhaus*, 188 USPQ 129, CCPA 1975.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21-36 are rejected under 35 U.S.C. 112, first paragraph, for scope of enablement because the specification, while being enabling the instant compounds for treating particular metabolic disorders or particular side effects (for example in claims 30-31) in a person induced by the treatment of the person with the particular known HIV protease inhibitor such as Ritonavir, Indinavir, or Amprenavir (see page 29 of the specification), does not reasonably provide enablement for treating **any** metabolic disorders which read on any disorders/disease in a person induced by the treatment of the person with **any** HIV protease inhibitors encompassing any known and unknown HIV protease inhibitors. Moreover, the specification, while being enabling the particular additional form of treatment for insulin resistance, hyperglycermia and disorders in claims 31 for the method of treatment herein, does not reasonably provide enablement for treating **any** agents represented by an additional form of treatment for insulin resistance, hyperglycermia and disorders herein.

These recitations, "an HIV protease inhibitor", "an additional form of treatment for insulin resistance, hyperglycermia ...", are seen to be merely functional language.

The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without ***undue experimentation***. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

The nature of the invention: The instant invention pertains to a method of treating metabolic disorder in a person induced by the treatment of the person with an HIV protease inhibitor.

The relative skill of those in the art: The relative skill of those in the art is high.

The breadth of the claims: The instant claims are deemed very broad since these claims reads on **any** metabolic disorders in a person induced by the treatment of the person with **any** HIV protease inhibitors encompassing any known and

unknown HIV protease inhibitors and in combination any agents for treating insulin resistance, hyperglycermia and disorders herein.

The amount of direction or guidance presented:

Functional language at the point of novelty, as herein employed by Applicants, is admonished in *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (CAFC, 1997). The CAFC clearly states that "[A] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials" at 1405(emphasis added), and that "It does not define any structural features commonly possessed by members of the genus that distinguish from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus.." at 1406 (emphases added).

In the instant case, "an HIV protease inhibitor", "an additional form of treatment for insulin resistance, hyperglycermia ...", recited in the instant claims are purely functional distinction. Hence, these functional recitations read on any compounds that might have the recited functions. However, the specification merely provides those agents for each kind of functional compounds for the claimed method of treatment herein.

Thus, the instant specification fails to meet the requirements set forth under 35 U.S.C. 112, first paragraph, since it fails to provide those elements

required to practice the inventions, nor "inform the public during the life of the patent of the limited of monopoly asserted" (*General Electric Company v. Wabash Appliance Corporation et al.* 37 USPQ at 468 (US Supreme Court 1938)).

The predictability or unpredictability: the instant claimed invention is highly *unpredictable* as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art cannot fully described genus, visualize or recognize the identity of the members of the genus, by structure, formula, or chemical name, of the claimed subject matter, except those particular compounds of formula disclosed in the specification, as discussed above in *University of California v. Eli Lilly and Co.* Hence, in the absence of fully recognizing the identity of the members genus herein, one of skill in the art would be unable to fully predict possible physiological activities of any compounds having claimed functional properties in the claimed method of treatment herein.

Moreover, one skilled in the art would clearly recognize that the recitation "a metabolic disorder in a person induced by the treatment of the person with an HIV protease inhibitor" encompasses any disease states or conditions or side-effects induced by the treatment of the person with any HIV protease inhibitor, a

great numbers of diseases or disorders, which would be *involved various, many possible, and different, separate and independent etiologies*. Thus, the skilled artisan would view that the treatment of all conditions states or conditions or side-effects induced by the treatment of the person with any HIV protease inhibitor by administering the particular compound herein is **highly unpredictable**.

Moreover, one of skill in the art would recognize that it is highly unpredictable in regard to therapeutic effects for treatment herein in a person, side effects, and especially serious toxicity that may be generated by drug-drug interactions when and/or after administering to a person the *combination* of the instant compound, and any HIV protease inhibitor, and further in combination any agents for treating insulin resistance, hyperglycermia and disorders herein. See text book "Goodman & Gilman's The Pharmacological Basis of Therapeutics" regarding possible drug-drug interactions (9th ed, 1996) page 51 in particular. This book teaches that "The frequency of significant beneficial or adverse drug interactions is unknown" (see the bottom of the left column of page 51) and that "Recognition of beneficial effects and recognition of and prevention of adverse drug interactions require a thorough knowledge of the intended and possible effects of drugs that are prescribed" and that "The most important adverse drug-drug interactions occur with drugs that have serious toxicity and a low therapeutic index, such that relatively small changes in drug level can have significant adverse consequences" (see the right column of page 51) (emphases added).

In the instant case, in the absence of fully recognizing the identity of the members genus of HIV protease inhibitor and agents for treating insulin

resistance, hyperglycermia and disorders herein except those particular agents in the specification, one of skill in the art would not be able to fully predict the possible treatments herein and possible adverse effects occurring with many compounds having claimed functional properties and their combinations to be administered to a host in the claimed method herein. Thus, the teachings of the "Goodman & Gilman's" book clearly support that the instant claimed invention is highly unpredictable.

The presence or absence of working examples and the quantity of experimentation necessary:

It is noted that the testing data in working examples merely show the particular metabolic disorders induced by the particular HIV protease inhibitor (see page 29 of specification). Thus, the evidence in the examples is also not commensurate in scope with the claimed invention and does not demonstrate criticality of a claimed range of treating **any** metabolic disorders in a person induced by the treatment of the person with **any** HIV protease inhibitors encompassing any known and unknown HIV protease inhibitors and in combination any agents for treating insulin resistance, hyperglycermia and disorders herein. See MPEP § 716.02(d).

Thus, the specification fails to provide clear and convincing evidence in sufficient support of the broad use of any compounds having those functions recited in the instant claims. As a result, necessitating one of skill to perform an exhaustive search for the embodiments of treating **any** metabolic disorders in a person induced by the treatment of the person with **any** HIV protease inhibitors

and in combination any agents for treating insulin resistance, hyperglycermia and disorders herein recited in the instant claims suitable to practice the claimed invention.

Genentech, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the *Wands* factors, the case *University of California v. Eli Lilly and Co.* (CAFC, 1997) and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in *undue experimentation* to test all agents and diorders encompassed in the instant claims and their combinations to be administered to a person employed in the claimed methods of the particular treatments herein, with no assurance of success.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 32 and 34-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation, "insulin analog" render these claims indefinite. The recitation, "insulin analog" are not defined in the specification. Hence, one of ordinary skill in the art could not ascertain and interpret the metes and bounds as to "insulin analog" encompassed thereby.

The recitation " less than the amount of the additional form of treatment" renders these claims indefinite since "less" is a relative term. Hence, one of ordinary skill in the art could not ascertain and interpret the metes and bounds of the patent protection desired as to " less than the amount of the additional form of treatment" " encompassed thereby.

The terminal disclaimer filed on December 17, 2003, disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of U.S. 6,458,998 has been reviewed and is accepted. The terminal disclaimer has been recorded. Therefore, the obviousness-type double patenting rejection of record stated in the previous Office Action dated is withdrawn.

In view of the rejections to the pending claims set forth above, no claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is 571.272.0627. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on 571.272.0629. The fax phone number for the organization where this application or proceeding is assigned is 703.872.9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-1235.

S. Anna Jiang, Ph.D.
Patent Examiner, AU 1617
March 15, 2004